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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,043	02/04/2005	Paul Howley	23117	4403

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EXAMINER	
BLUMEL, BENJAMIN P	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,043	HOWLEY ET AL.	
	Examiner	Art Unit	
	BENJAMIN P. BLUMEL	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-60* is/are pending in the application.

4a) Of the above claim(s) *41-44, 46, 47 and 57-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-40,45,48-56 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/6/07 & 2/4/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants are informed that the rejections of the previous Office action not stated below have been withdrawn in view of the Applicant's arguments and/or amendments. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 4, 2008 has been entered.

Claims 32-40, 45, 48-56 and 60 are examined on the merits. Claims 41-44, 46, 47 and 57-59 remain withdrawn from consideration as non-elected inventions.

Response to Arguments

Applicant's arguments with respect to claims 32-40, 45, 48-56 and 60 have been considered but are moot in view of the new ground(s) of rejection. However, responses to arguments pertaining to re-cited references are provided below.

Claim Rejections - 35 USC § 102

(New Rejection) Claims 49, 50 and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Baxby and Rondle (Archives of Virology, 1967), as evidenced by Antoine et al. (Virology, 1998).

The claimed invention is drawn to an isolated avian cell comprising a vaccinia virus gene of non-integrated DNA, such as C7L or K1L or a homologue of said gene, but is not part of a vaccinia virus genome.

Baxby and Rondle teach the titering of cowpox viruses (CPX) in chicken embryonic fibroblasts (CEFs). Since cowpox virus contain homologues of vaccinia C7L (CPX orf G3L) and K1L (CPX orf M1L) as evidenced by Antoine et al., see table 1, the instant invention is anticipated by Baxby and Rondle.

Claim Rejections - 35 USC § 103

(New Rejection) Claims 32-40, 45, 56 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tartaglia et al. (US 6,004,777), Cochran and Junker (US 6,294,176), Antoine et al. (Virology, 1998).

The claimed invention is drawn to a recombinant avipoxvirus that contains a host range gene of vaccinia virus or a homologue thereof, which results in an increased titer compared to a virus without the host range gene and an isolated avian cell containing the recombinant

avipoxvirus. The avipoxvirus contains vaccinia virus host range genes C18L, C17L, C7L, K1L, B4R, B23R or B24R or homologues thereof. The recombinant avipoxvirus can also express heterologous gene, such as an antigen or a therapeutic compound, as part of a vaccine composition. The recombinant avipox of the instant invention is designed to produce an immune response in a human and can be cultured in avian cells.

Tartaglia et al. teach an immunological composition of recombinant poxviruses (fowlpox and canarypox) that express heterologous antigens, such as HIV antigens *gag-pro*, gp120/TM, and Nef/Pol poly-epitope string. Tartaglia et al. discuss the improved expression of heterologous antigens through the insertion of translation factors into the genome of recombinant poxviruses. The translation factors can be the open reading frames of: E3L, K3L, VAI RNA, EBER RNA, sigma 3, TRBP, a homolog thereof, and combinations thereof. Tartaglia et al. teach that the preferred translation factors are the Vaccinia E3L and K3L (host range genes), which can be inserted in combination or separately into the recombinant poxvirus genome in order to enhance heterologous gene expression. Tartaglia et al. further teach that CEFs (avian cells) can be used in replicating ALVAC based viruses. However, Tartaglia et al. do not teach the generation of avipox viruses with vaccinia K1L or C7L.

Cochran and Junker teach the generation of recombinant raccoonpox and swinepox viruses. Cochran and Junker insert the host range genes C7L and K1L from raccoonpox viruses into Swinepox in order to increase the cellular tropism for target cells since Swinepox do not contain the K1L gene. Cochran and Junker also teach that raccoonpox viruses have been used in inducing immune responses various animals, including avian species and that fowlpox or

canarypox viruses can also be modified by the insertion of raccoonpox virus promoters E11L or I5L in order to express heterologous DNA.

Antoine et al. teaches the complete genome of the MVA virus and its comparison to other Orthopoxviruses. Antoine et al. identifies the hose range genes C17L, C18L, C7L, K1L, B4R, B23R or B24R at the open reading frames of 3L and 4L (C17L/B23R), 18L (C7L), 22L (K1L), 171R (B4R) and 190R (B23R). *See table 1.*

It would have been obvious to one of ordinary skill in the art to modify the composition taught by Tartaglia et al. in order to generate an avipoxvirus with a vaccinia virus host range gene inserted into the avipoxvirus genome. One would have been motivated to do so, given the suggestion by Tartaglia et al. that either CPV or FPV can be modified by inserting the vaccinia virus E3L host range gene or a homologue thereof into either of the avipoxvirus genomes in order to increase expression of heterologous genes. There would have been a reasonable expectation of success, given the knowledge that similar host range gene insertion (C7L or K1L) from one species of orthopoxvirus (raccoonpox) to distinct orthopoxvirus (swinepox), as taught by Cochran and Junker, and also given the knowledge that the vaccinia virus host range genes C17L, C18L, C7L, K1L, B4R, B23R and B24R were identified and sequence from MVA virus, the same virus utilized in the specification, prior to the claimed invention, as taught by Antoine et al. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to arguments:

Applicants argue that Tartaglia et al. do not teach an avipoxvirus that expresses vaccinia virus genes C17L, C18L, C7L, K1L, B4R, B23R or B24R. Furthermore, Tartaglia et al. do not

teach increased titers of their recombinant avipoxvirus that expresses Vaccinia virus E3L and/or K3L since their research focused on increased expression of heterologous genes. In addition, it is argued that the examiner's interpretation of "homologue thereof" (see claim 32) based on the specification is incorrect since the sequences alignments between that of vaccinia E3L and K3L and the genes of claim 32 reveals sequence mis-matches, therefore, E3L and K3L are not the same as the genes of claim 32.

In response, it is acknowledged that Tartaglia et al. do not teach inserting vaccinia virus C17L, C18L, C7L, K1L, B4R, B23R or B24R into the genome of an avipoxvirus, nor the increased titer as a result of such an insertion. However, their research of inserting other host range genes into the genome of canarypox or fowlpox viruses (both avipoxviruses) does provide guidance and a reasonable expectation that other host range genes could be successfully inserted into avipoxvirus, given that these genes have been mapped with their nucleotide positions in vaccinia virus as taught by Antoine et al. Furthermore, based on the newly cited teachings of Cochran and Junker, one skilled in the art would be further motivated to insert C7L and/or K1L of one poxvirus into another distinct poxvirus in order to expand the recipient poxviruses cellular tropism/host range. Therefore, even if the intent was not focused on higher viral titers, any avipoxvirus receiving the host ranges genes of Cochran and Junker or Antoine et al. would posses the ability to have increased viral titers.

Applicants also argue that Antoine et al. do not teach an avipoxvirus with the vaccinia virus genes of claim 32 or a high viral titer of such an avipoxvirus.

In response, it is acknowledged that Antoine et al. do not teach these limitations, however, Antoine et al. do provide the genomic map of these claimed host range genes with

detail coding regions of each open reading frame, thereby providing guidance for one skilled in the art to explore additional genes relating to host range function as Tartaglia et al. have done.

Furthermore, the claimed recombinant avipoxvirus with vaccinia host range genes, achieves a higher titer as compared to an avipoxvirus only expressing a marker gene. However, the applicants have not compared this recombinant avipoxvirus with the closest prior art of Tartaglia et al. (US 6,004,777) as required by MPEP 716.02(e) "Comparison With Closest Prior Art [R-2]", which states, An affidavit or declaration under 37 CFR 1.132 must compare the claimed subject matter with the closest prior art to be effective to rebut a prima facie case of obviousness. In re Burckel, 592 F.2d 1175, 201 USPQ 67 (CCPA 1979).

(New Rejection) Claims 48-50 and 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tartaglia et al. (*supra*), Cochran and Junker (*supra*), Antoine et al. (*supra*).

The claimed invention is drawn to an isolated avian cell comprising recombinant avipoxvirus that contains a host range gene of vaccinia virus or a homologue thereof, which results in an increased titer compared to a virus without the host range gene and an isolated avian cell containing the recombinant avipoxvirus. The avipoxvirus contains vaccinia virus host range genes C18L, C17L, C7L, K1L, B4R, B23R or B24R or homologues thereof. This recombinant avipoxvirus results from the homologous recombination of an avipoxvirus with that of a vaccinia virus which are both in the isolated avian cell.

The teachings of Tartaglia et al., Cochran and Junker and Antoine et al. are discussed above. In addition, Tartaglia et al. and Cochran and Junker both teach the use of homologous recombination in order to generation recombinant avipoxvirus and swinepoxvirus, respectively.

Tartaglia et al. employ such a method for inserting HIV antigens and vaccinia E3L and/or K3L, while Cochran and Junker use it to insert C7L and/or K1L into swinepoxviruses.

It would have been obvious to one of ordinary skill in the art to modify the composition taught by Tartaglia et al. in order to generate an avipoxvirus with a vaccinia virus host range gene inserted into the avipoxvirus genome through homologous recombination. One would have been motivated to do so, given the suggestion by Tartaglia et al. that either CPV or FPV can be modified by inserting the vaccinia virus E3L host range gene or a homologue thereof into either of the avipoxvirus genomes in order to increase expression of heterologous genes through homologous recombination. There would have been a reasonable expectation of success, given the knowledge that similar host range gene insertion (C7L or K1L) from one species of orthopoxvirus (raccoonpox) to distinct orthopoxvirus (swinepox) through homologous recombination, as taught by Cochran and Junker, and also given the knowledge that the vaccinia virus host range genes C17L, C18L, C7L, K1L, B4R, B23R and B24R were identified and sequence from MVA virus, the same virus utilized in the specification, prior to the claimed invention, as taught by Antoine et al. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(New Rejection) Claims 32-40, 45, 48-56 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 49 recites, "...comprising a

Vaccinia virus host range gene selected from the group consisting of...wherein the host range gene is not part of a Vaccinia virus genome.", however, it is unclear how a vaccinia virus host range gene can not be part of a vaccinia virus genome. If applicants are attempting to claim that the virus is not present in the cell but the genes are, perhaps amending the claim to recite, "...comprising isolated Vaccinia virus host range genes..." or "...comprising an individual host range gene isolated from a vaccinia virus genome..." would clarify what is required to be in the cell. Claims 50-55 are rejected since they depend from a rejected claim.

Claims 32 and 48 recite, "...having an increased viral titer compared to that of a corresponding avipoxvirus without said Vaccinia virus host range gene..." and "...a recombinant avipoxvirus...contains the vaccinia virus host range gene, has an increased viral titer over that of a corresponding avipoxvirus without said vaccinia virus host range gene...", respectively. However, referring to something that is variable and can't be determined makes the claimed invention indefinite based on the guidance of MPEP § 2173.05 (b). In light of this section of the MPEP, that claimed invention referencing increased viral titer as compared to a corresponding avipoxvirus can be achieved by concentrating one viral preparation and/or diluting another resulting in differences in viral titers. In addition, since claims 32 and 48 also recite the involvement of avian cells in replicating avipoxviruses, this too contains variables, such as growth conditions of cells, length of viral production in cells, etc. Claims 33-40, 49-52, 56 and 60 are rejected since depend from either claims 32 or 49.

Claim 51 recites, "...wherein the host range gene is integrated in the cellular genome.", however, it is unclear how the host range gene can be in the vaccinia virus as recited in claim 48 and integrated in the host cell genome.

Claim 55 recites, "…wherein the host range gene...is not part of the genome of the avipoxvirus.", however, it is unclear how the host range gene can be part of the avipoxvirus genome as recited in claim 48 and then not be part of it as recited in claim 55.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "drug" in claim 40 is used by the claim to mean "a recombinant avipoxvirus", while the accepted meaning is "a chemical substance that affects the processes of the mind or body. Any chemical compound used in the diagnosis, treatment, or prevention of disease or other abnormal condition." (see Dorlands Medical Dictionary referenced in PTO-892). The term is indefinite because the specification does not clearly redefine the term.

Summary

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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